

04 March 2015

Treatment of primary liver cancer:

SARAH study completes enrolment, results expected late 2016.

Launched by the Assistance Publique – Hôpitaux de Paris in December 2011, ‘SARAH’ – the French national collaborative randomized controlled study of yttrium-90 resin microspheres versus sorafenib in advanced hepatocellular carcinoma (HCC) has enrolled more than 400 patients; results expected late 2016.

SARAH, a large French study of patients with advanced, inoperable primary liver cancer (hepatocellular carcinoma, or HCC) has completed patient enrolment, exceeding its 400-patient target, according to its principal investigator, Professor Valérie Vilgrain MD, PhD, Department of Radiology, Beaujon Hospital, Assistance Publique – Hôpitaux de Paris (AP-HP) and Université Paris Diderot, Sorbonne Paris Cité, France.

The randomized controlled SARAH study, sponsored by the AP-HP, directly compares the efficacy of selective internal radiation therapy (SIRT, also known as radioembolization) using yttrium-90 [Y-90] resin microspheres (SIR-Spheres[®] Y-90 resin microspheres, Sirtex Medical Limited, Sydney, Australia) versus sorafenib (Nexavar[®], Bayer HealthCare Pharmaceuticals, Berlin, Germany), a systemic therapy that is the current standard of care for patients with inoperable advanced HCC. “SARAH is the largest randomized study ever to compare selective internal radiation therapy – or any liver-directed therapy – against the standard-of-care systemic therapy in the treatment of primary liver cancer. The SARAH study team is delighted that enrolment is now complete, with results expected in late 2016,” Prof. Vilgrain said.

SARAH (SorAfenib versus RAdioembolization in AAdvanced HHepatocellular carcinoma) is a Phase III multi-centre prospective randomized open-labelled study for patients in France with advanced HCC (Barcelona Clinic Liver Cancer stage C) with or without portal vein thrombosis

and no extrahepatic spread, or whose disease has progressed or recurred after previous therapies; and who are ineligible for surgical resection, ablation or liver transplantation.^{1,2}

The primary goal of the SARAH study is to assess if radioembolization with Y-90 resin microspheres provides an increased survival benefit compared to sorafenib in patients with advanced HCC. The study is also comparing the quality of life of patients and other measures such as the tolerability of the treatments.

Coordinated by Professor Valérie Vilgrain, more than 25 specialist cancer centres throughout France are involved in this study. SIR-Spheres Y-90 resin microspheres were selected for the test arm of this independent, collaborative national study. “Target enrolment was reached in around three years, which is remarkable for a single-country trial of this size in a hard-to-treat cancer with few proven therapeutic choices,” Prof. Vilgrain noted.

Sorafenib was established as the standard treatment for patients with advanced HCC following the results of the pivotal SHARP randomized controlled trial, which demonstrated an increased median overall survival from 8 to 11 months compared to placebo.³ However, 80% of patients receiving sorafenib also experienced treatment-related adverse events.

SIRT with SIR-Spheres Y-90 resin microspheres is an approved treatment for inoperable liver tumours. It is a minimally-invasive treatment that delivers high doses of high-energy beta radiation directly to the tumours. SIRT is administered to patients by interventional radiologists, who infuse millions of radioactive microspheres (diameter between 20–60 microns) via a catheter into the liver arteries that supply blood to the tumours. By using the tumours’ blood supply, the microspheres selectively target liver tumours with a dose of radiation that is up to 40 times higher than conventional radiotherapy, while sparing healthy tissue.

Interest in a randomized controlled study of SIRT using Y-90 resin microspheres in this patient population was based on a substantial number of open-label single-group studies as well as a large multi-centre European study on the long-term outcomes related to survival and safety of SIR-Spheres Y-90 resin microspheres in patients with inoperable HCC.⁴ In 13 open-label single-group studies with a total of 400 patients with advanced HCC, the combined estimation of the median overall survival after radioembolization with Y-90 microspheres was 15 months, with a range of 7–27 months.

Current Availability of SIR-Spheres Y-90 resin microspheres

SIR-Spheres Y-90 resin microspheres are approved for the treatment of inoperable liver tumors in Australia, the European Union (CE Mark), Argentina (ANMAT), Brazil, and several countries in Asia, such as India and Singapore. SIR-Spheres Y-90 resin microspheres also have a full Pre-Market Approval (PMA) by the FDA and are indicated in the United States for the treatment of

non-resectable metastatic liver tumors from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine.

About Hepatocellular Carcinoma

HCC typically occurs in people whose livers have become severely damaged or cirrhotic, due to conditions such as hepatitis or alcohol abuse. It is one of the ten most-common cancers in the world, with nearly 750,000 cases diagnosed annually, and the second most common cause of cancer deaths.⁵ It occurs with greatest frequency in regions where viral hepatitis B or C are most often diagnosed, such as in Asia Pacific and Southern Europe.

Hepatocellular cancer can be cured by surgery, either by resecting the diseased parts of the liver, or by transplantation with a liver from a healthy donor. However, the great majority of patients with HCC have disease which is too advanced for surgical interventions, and as a consequence their survival may range from a few months to two or more years depending largely on the state of their liver function at the time of their diagnosis and the extent of tumour invasion.

References:

1. Sorafenib versus Radioembolization in Advanced Hepatocellular carcinoma (SARAH):
<http://clinicaltrials.gov/ct2/show/NCT01482442>.
2. Vilgrain V, Abdel-Rehim M, Sibert A *et al*. Radioembolisation with yttrium-90 microspheres versus sorafenib for treatment of advanced hepatocellular carcinoma (SARAH): study protocol for a randomised controlled trial. *Trials* 2014; **15**: 474.
3. Llovet J, Ricci S, Mazzaferro V *et al* for the SHARP Investigators Study Group. Sorafenib in advanced hepatocellular carcinoma. *New England Journal of Medicine* 2008; **359**: 378–390.
4. Sangro B, Carpanese L, Cianni R *et al* on behalf of European Network on Radioembolization with yttrium-90 resin microspheres (ENRY). Survival after ⁹⁰Y resin microsphere radioembolization of hepatocellular carcinoma across BCLC stages: A European evaluation. *Hepatology* 2011; **54**: 868–878.
5. GLOBOCAN. Liver Cancer Incidence and Mortality Worldwide in 2012.
http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx accessed 10 February 2015.

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